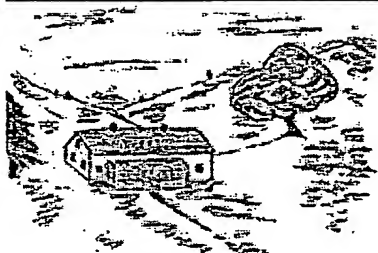


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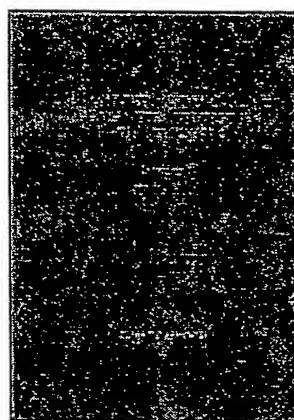
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Adhesives Applications and Properties
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The chapters in this book cover a wide and diverse range of topics, providing a detailed discussion of each.

From the Preface: "Pressure sensitive adhesive science and technology is still a rapidly growing field and new information continues to be developed. Our understanding of pressure sensitive properties and their testing is improving, new materials are still being developed and find applications in the pressure sensitive adhesive technology and the new uses of pressure sensitive adhesives and related materials are expanding. The purpose of this series is to present the material in a greater detail than is possible or desirable during technical meetings or in the periodical literature...Greater detail is always of value to the technologist directly involved in product development, product manufacturing or other activities..."

Target Audience: Highly recommended for all professionals, especially researchers, using or formulating pressure sensitive adhesives.

Table of Contents:

Tack in Adhesive Bond Making

Rheology of Pressure Sensitive Adhesives

Application of Dielectric Analysis in the Design of Delayed Action Heat Seal and Pressure Sensitive Adhesives

Mechanical Property—Performance Relations of Acrylic Pressure Sensitive Adhesives

The Use of Amorphous Polyalphaolefins in the Formulation of Hot Melt Pressure Sensitive Adhesives

Silicone Pressure Sensitive Adhesives for Healthcare Applications

Wound Dressings

Repulpable Pressure Sensitive Adhesives

Drying of Aqueous Coatings

Index

Note: *Advances in Pressure Sensitive Adhesive Technology — 3* is a companion volume to this title.

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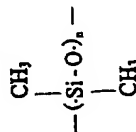
Many of the unique properties of silicones have made them ideal for various applications in the healthcare industry. Initial uses of silicone adhesive in this industry included tapes, dressings and bandages. In addition, the adhesives were used for attaching devices to the skin (e.g. ostomy seals) or for attaching prosthetic devices to the body. Also, the silicone pressure sensitive adhesives, by meeting the requirements of a pharmaceutical excipient, have benefited from the development of transdermal drug delivery systems since the turn of the 1970s. Recently, an improved understanding of the skin adhesion and high permeability of some silicone gels have allowed them to be used with success in new fields of wound care applications.

The molecular structure, bond strength and physicochemical behavior form the basis for understanding their unique properties and the reason why they have become so indispensable in many applications [1].

Physical and chemical properties of silicone adhesives will be explored in this chapter as well as the characteristics of silicones that enable them to satisfy both pressure sensitive adhesive needs and the needs of new and emerging medical requirements. Initially, an overview of the structure chemistry and properties of silicone pressure sensitive adhesives is discussed. To provide insight into what types of applications these adhesives are utilized in, various examples of their use in healthcare applications are summarized. Finally, in an attempt to expand the current scope of silicone pressure sensitive adhesive technology, a review of new and emerging developments and/or improvements of silicone pressure sensitive adhesives is provided.

STRUCTURE AND PROPERTIES OF SILICONES

The term silicone is currently an alternative name for polyorganosiloxane, and more frequently for polydimethylsiloxane as shown below [2]:



Polydimethylsiloxanes have a semi-organic molecular structure in which an inorganic silica-like backbone supports a regular arrangement of pendant methyl groups. The key property of the backbone is its flexibility and the key property of the organic group is its intrinsic surface activity [3]. In fact, the siloxane chain has an extremely open macromolecular structure, large backbone bond angles, long bond lengths, divalent oxygen and freedom of rotation about bonds, all of which supports its high and unique flexibility. In addition, as shown in Table 30-1, the siloxane chain is slightly polar with a high bond energy.

30. SILICONE PRESSURE SENSITIVE ADHESIVES FOR HEALTHCARE APPLICATIONS

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INTRODUCTION

The applications of silicones are varied and essential to many industries. The electronics industry owes its tremendous and fast progress to the inorganic derivatives of silicon, the semi-organic form of silicon, currently known as silicones, largely contributed to the development and success of silicon's chemistry. The initial synthesis and use of silicones as oils and resins began in the 1940s and today silicones have expanded into almost every market. Various applications involving synthetic materials have utilized silicone technology. All of this was possible because of the versatile nature of silicones which are available as volatile liquids and as heavier fluids, gums, and elastomers. They can perform as surfactants, lubricants, coatings, adhesives and sealants. Moreover, in many cases silicones have become essential and even irreplaceable. For instance, the pressure sensitive adhesives industry recognizes silicones as one of its key materials, using its intrinsic surface properties in the design of release coatings universally used for protection of adhesive in labels. However, viscoelastic characteristics also allow silicones to be used as pressure sensitive adhesives.

Table 30-1. Molecular Characteristics of Polymethylsiloxanes

| Energy of Rotation About Bonds | | |
|--------------------------------|-------------------------|-------------|
| carbon-to-carbon | polystyrene | 13.8 kJ/mol |
| | polytetrafluoroethylene | 19.7 kJ/mol |
| silicon-to-oxygen | polydimethylsiloxane | 0 kJ/mol |
| Bond Angles | | |
| Si-O-Si | organosiloxanes | 105°-180° |
| | hexamethyldisiloxane | 130° |
| C-O-C | dimethylether | 111° |
| C-C-C | propane | 112° |
| Bond Lengths | | |
| Si-O | hexamethyldisiloxane | 0.163 nm. |
| C-O | dimethylether | 0.142 nm |
| C-C | propane | 0.154 nm |
| Bond Energies | | |
| carbon-to-carbon | | 356 kJ/mol |
| silicon-to-oxygen | | 444 kJ/mol |
| silicon-to-carbon | | 314 kJ/mol |

Since the energy required for bond rotation is nearly zero, the flexibility of the siloxane backbone chain is truly unique. This freedom of rotation allows for the polymer orientation to consist of both an inorganic backbone (high surface energy) with a pendant methyl group array (low surface energy). The pendant methyl groups form a regular, apolar, hydrophobic arrangement which develops very low intermolecular interactions and unique surface characteristics. These characteristics are greatly enhanced by the ability of the backbone to spread out the methyl substitution at interfaces. That results in very low surface energies as shown in Table 30-1. Often times, methyl groups are substituted by other organic groups such as hydrogen, hydroxyl, vinyl, phenyl, alkoxy, fluoroalkyl, polyethylene oxide, etc., in order to modify specific properties of the siloxane polymer. Substitution with other organic groups often provides enhanced or modified reactivity, adhesion, surface energy, thermostability, hydrophilicity, etc.

The consequences of this unique molecular structure are summarized in Table 30-2. When working with pressure sensitive adhesives, the two key characteristics are: 1) the ability of the silicone polymer to wet virtually any

surface and to spread on a wide variety of substrates and 2) suitable viscoelastic behavior, when silicone resin is incorporated, which provides tack, adhesion, cohesive strength and easy peel release by adhesive failure.

Table 30-2. Physico-Chemical Properties of Polydimethyl Siloxanes of Varying Molecular Structure

| PROPERTIES | ORIGIN |
|--|---|
| Surface active characteristics | |
| Critical surface tension of wetting | 24 mN/m |
| Liquid surface tension (at 20°C) | 20.4 mN/m |
| Glass transition temperature (T _g) | |
| Polydimethylsiloxane | 146K |
| Polyethylene | 148K |
| Polytetrafluoroethylene | 160K |
| Polyisobutylene | 200K |
| Ability to have rubbery behavior | Chain flexibility and mobility |
| Elastomer properties of crosslinked structure at room temperature | Open structure |
| Flowability, ability to form a film | Apolarity and hydrophobicity of pendant methyl groups |
| Ability to spread out on a wide variety of substrates | Very low molecular interactions |
| Lubricating, antifoaming, waterproofing, release | |
| Lowest surface shear viscosity | |
| High gas permeability | |
| Highest permeability coefficient for N ₂ and O ₂ | |
| Constant physical properties within a wide temperature range | |
| Excellent dielectric properties | |
| Intra- and intermolecular reactions made easier | |
| Good thermooxidative stability | High Si-O homolytic stability |
| Chemical inertness to many substances | |
| Good resistance to high temperatures | Good stability of Si-C |
| Sensitivity to acids and bases (hydrolysis) | Absorption of methyl groups under 300 nm |
| Transparency, good light stability | |
| Biocompatibility | |

SYNTHESIS AND MANUFACTURING

Like many other pressure sensitive adhesives, silicone pressure sensitive adhesive formulations are based on resin and polymer. Flowable polydimethylsiloxane polymers can be prepared at a variety of viscosities and like other polymer systems, the viscosities are dependent upon the chain length. The smallest and the least viscous siloxane entity is hexamethyldisiloxane (0.65 cSt), which is volatile. The highest molecular weight species take the form of gums; however, even at these high molecular weights the pure linear polydimethylsiloxane does not have pressure sensitive adhesive properties. The polymers must be reinforced and tackified by a resin to gain their essential viscoelastic properties.

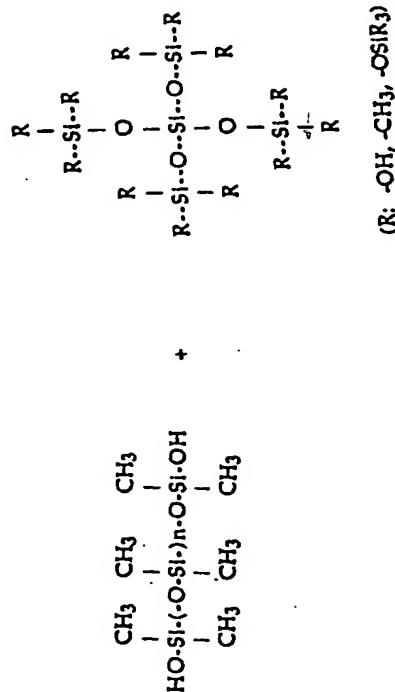


Fig. 30-1. Dimethyl siloxane polymer and silicate resin.

As shown in Figure 30-1 the tackifying resin consists of a soluble, three dimensional trimethylsiloxy and hydroxy end-blocked silicate structure. Simply blending the polymer and the resin (by dissolving them into a hydrocarbon solvent and removing the solvent) will often provide some pressure sensitive adhesive properties (e.g. tack and adhesion); however, unless polymer and resin are covalently bound together, poor cohesive properties typically result. Improving the cohesive strength of the pressure sensitive adhesive requires incorporation of crosslinks into the polymer network. Higher crosslink densities often result from the condensation of silanol groups present on both the polymer and the resin; however, other functional groups can also be incorporated onto the resin and/or polymer structure (e.g. $\text{-SiH}_2\text{-SiCH=CH}_2\text{-}$, -SiOR, etc.). In addition, the use of catalysts for reinforcing the siloxane network and improving the

The cohesive strength of silicone adhesive has been documented [4]. The three types of catalysts most commonly employed for industrial applications are organic peroxides (e.g., benzoyl peroxide or 2,4-dichlorobenzoyl peroxide), amino silanes (utilized when a lower temperature cure is desired), and metal salts of organic acids.

The two most important factors in determining the performance characteristics of silicone adhesives are the resin to polymer ratio and the degree of crosslinking [5]. A minimum concentration of resin is required to tackify the polymer so that it exhibits pressure sensitive adhesive properties; however, too much resin will result in poor tack and loss of adhesion.

Figure 30-2 illustrates the chemistry of two families of silicone pressure sensitive adhesives which were found useful in health care applications.

Both families begin with the condensation reaction between a hydroxy end sensitive adhesives which were found to be used as a means of controlling the polymerization of the resin. The standard adhesives manufactured and hydroxy end blocked silicate resin. The standard adhesives manufactured by this process contain a relatively high degree of silanol functionality. The silanol content of the adhesive can be significantly reduced by subsequently reacting the residual silanol groups with a trimethylsilyl endcapping agent. This family or adhesives is often referred to as amine compatible and exhibits enhanced chemical stability, especially in the presence of amine drugs [6,7]. The processing conditions (e.g. resin -to-polymer ratio, solvent concentration, catalyst type, end-blockers, temperature and time) can be adjusted to optimize the polycondensation reaction in order to achieve the desired pressure sensitive characteristics for a specific application.

Formulation

During the past three decades, silicone pressure sensitive adhesives, utilized by the healthcare industry, were soluble networks of polydimethylsiloxanes crosslinked with silicate resin [8,9]. The applications that these adhesives supported did not require their formulations to include catalysts, organic tackifiers, plasticizers, antioxidants, stabilizers or other potentially toxic extractables. The adhesives were supplied and applied as solutions which utilized available solvent coating techniques. Removal of the solvents resulted in silicone networks which exhibited typical pressure sensitive adhesive properties (e.g. tack, adhesion, cohesiveness and peel release) and exhibited excellent skin compatibility [10].

Tape Properties

In selecting a suitable adhesive for use in both medical and pharmaceutical applications the physical property requirements for the adhesive (e.g. tack, skin adhesion, release force, creep resistance, cohesive strength, permeability etc.) need to be balanced against the end use requirements (e.g. wear for extended

periods of time, wear during high stress activities, repeated application and removal, etc.) and performance criteria (e.g. non-irritating, non-sensitizing or hypoallergenic, chemically inert and exhibiting a moderate adhesion). Although many industrial silicone adhesives are available, relatively few of them meet these requirements due to both their aggressive adhesive properties (high adhesion, tack and cohesion) and/or their use of catalysts which could introduce cumulative or local systemic toxicity. However, similar to their industrial analogs, the two most important factors in determining the balance of performance properties of medical adhesives are the ratio of resin to polymer used in the pressure sensitive adhesive formulation and the level of silanol functionality present on both the resin and polymer. Utilizing the chemistry shown in Figure 30-2, increasing the polymer content (elastic component of modulus) yields an adhesive with higher tack, less shear strength and higher release. Subsequently, increasing the resin level (viscous component of the modulus) yields an adhesive with reduced tack, higher cohesive strength and increased adhesion.

For a given resin-to-polymer ratio, a higher level of silanol functionality will improve cohesive strength but will slightly decrease the tack and adhesion [4]. The bulk properties are also dependent on the molecular characteristics of polymers and resins (molecular weight, branching).

In summary, silicone adhesives can be manufactured to meet a wide range of pressure sensitive adhesive properties (e.g. tack, peel adhesion, peel release force, cohesive strength). In addition, they can also be customized to meet other user requirements by adjusting their processing properties (e.g. type of solvent, percent non-volatile content, solution viscosity, etc.).

Inherent Characteristics of Silicone Adhesives

Since silicone pressure sensitive adhesives are primarily based on polydimethylsiloxane materials, they have very low transition temperatures and good thermo-oxidative stability, as shown in Table 30-2. These properties allow silicone adhesives to maintain usable physical properties over a wider temperature range than their analogous organic counterparts. Also, their superior surface activity and enhanced ability to conform makes them the adhesive of choice for many substrates with low surface energy and irregular surface shapes. Although not often important for medical applications, silicone adhesives have very good electrical properties, maintain high dielectric strength, demonstrate good arc resistance and display low loss factors [4]. Silicone adhesives are also resistant to moisture, UV radiation, oxidative and biological attacks. In addition, silicone adhesives targeted towards both medical and pharmaceutical applications have been thoroughly tested on animal and human subjects and shown not to produce skin irritation or systemic toxicity, they can be formulated to adhere to the skin for extended periods of time, they can be easily removed without discomfort [10], and they can be formulated to provide

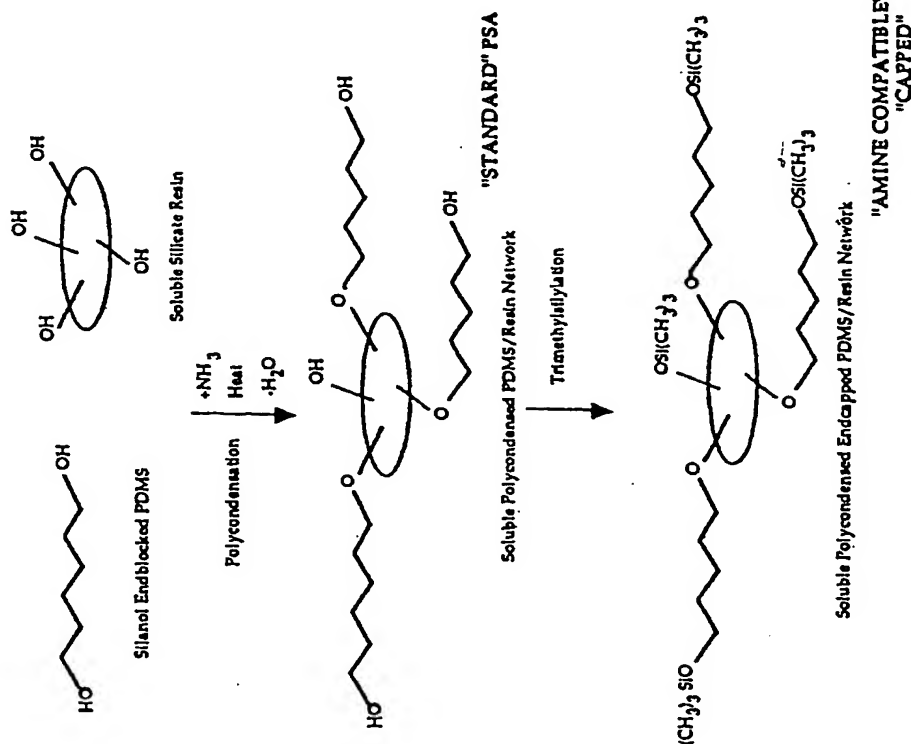


Fig. 30-2. Synthesis and structure of silicone pressure sensitive adhesives.

various rates of drug permeability, thus allowing a controlled rate of delivery to a patient over an extended period of time in transdermal drug delivery systems.

INDUSTRIAL APPLICATIONS

Electrical applications comprise the largest market segment for industrial silicone pressure sensitive adhesives. For instance, they are used as masking tapes in the manufacturing process of printed circuit boards where they protect the circuits against chemical attack during their immersion into treating solutions, soldering baths and air jets at high temperatures. Silicone pressure sensitive adhesives are also particularly suitable for aerospace and automotive applications that require cold weather performance balanced with rapid cycling to very high temperatures [11]. In addition, they are used in conjunction with glass fabric, fluorocarbon and other polymer plastic films for making insulation tapes which are used to protect electrical components in appliance motors and aircraft engines.

As a result of their low surface energy and ease of spreading (wetting), they are often used in applications which require bonding of low surface energy substrates such as fluorocarbon polymers, silicone rubbers and silicone coated materials. They are also utilized as process aids where tapes have to be resistant to long term exposure at high temperatures (200°C) and where protective tapes need to be easily removed without transferring.

HEALTHCARE APPLICATIONS

Medical pressure sensitive adhesives are a special class of pressure sensitive adhesives targeted towards use in a variety of healthcare applications (e.g. wound management, surgery, prosthesis, biomedical devices and pharmaceuticals).

Many of the typical properties developed for industrial pressure sensitive adhesives are also utilized as performance requirements for medical pressure sensitive adhesives; the latter differ from their industrial counterparts in that they have to adhere to and be easily removed from human skin. The adhesives are often used to attach and bond various systems as diverse as medical devices, electrodes, prostheses, dressings, pharmaceutical and transdermal therapeutic patches, topical plasters, cosmetic patches, wigs, and facial masks onto skin. In order to assure that they are suitable for prolonged skin contact applications, these pressure sensitive adhesives have some specific requirements which are outlined below in Table 30-4.

Table 30-4. Criteria for Intended Transdermal Applications of Pressure Sensitive Adhesives

| | |
|--|--|
| BIOCOMPATIBILITY | |
| Biologically inert | |
| Non-toxic (systemic toxicity), non-irritating, non-sensitizing, non-genotoxic | |
| Low level of potential extractables (organic plasticizers, tackifiers, stabilizers) | |
| EFFICACY | |
| Suitable tack for quick bonding to all skin types (dry, wet, oily) | |
| Suitable adhesiveness and cohesiveness | |
| Ability to conform to skin relief | |
| Adhesion to the skin for extended period of time | |
| Easily removable from skin without causing trauma, discomfort, and residue | |
| Permeable to a wide range of therapeutic substances and gases (O ₂ , water vapor) | |
| STABILITY | |
| Good chemical inertness | |
| Good compatibility with drugs and galenic excipients | |
| Ability to retain physico-chemical properties at skin temperatures | |
| MANUFACTURING | |
| Easily fabricated | |
| Manufacturing in accordance with GPM | |
| FORMULATION | |
| Easily customized | |
| Easily co-formulated | |
| Easy to process | |

Transdermal Drug Delivery Systems

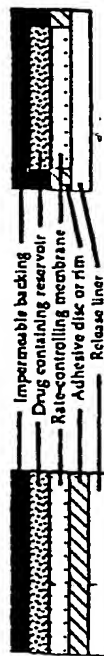
An expanding market for the use of medical pressure sensitive adhesives is their use in pharmaceutical delivery systems which administer active substances via transdermal drug delivery systems. Transdermal drug delivery systems have been recognized and developed for administering systemic medications and local therapy. They provide the advantages of a direct and controlled entry of a pharmaceutical into the blood circulation, in addition, they have enhanced patient use because they maintain a constant and prolonged therapeutically effective drug level while bypassing hepatic first pass metabolism [12,13].

As shown in Figure 30-3, different types of construction are often used to make transdermal drug delivery systems [14].

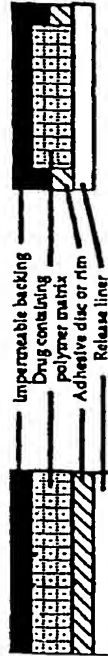
In both the reservoir and polymer matrix devices, medical adhesives are used to adhere the patch onto the skin. The adhesive film must be inert and highly permeable to the active substances. It can cover either the entire skin contact surface or only the edge of the patch and the final design is typically

selected according to the compatibility of the adhesive with the components of the formulation. The adhesive matrix device is the simplest type of transdermal drug delivery system. The pressure sensitive adhesive matrix is required to provide storage of active substances, control over their delivery rate and partitioning into the stratum corneum and skin adhesion.

RESERVOIR SYSTEM:



POLYMER MATRIX SYSTEM:



ADHESIVE MATRIX SYSTEM:



Fig. 30-3. Cross sectional representation of three basic designs for transdermal drug delivery devices.

The adhesive plays a key role in the system design by ensuring intimate and safe contact of the patch with the skin surface, thus allowing the drug to penetrate the stratum corneum under optimal conditions. In addition to tape properties, the selection of optimal adhesive involves the following biological and technical criteria: biocompatibility, efficacy, stability, ease of fabrication and modification.

Biocompatibility

Silicone pressure sensitive adhesives are recognized as suitable for use in transdermal drug delivery systems by complying with the requirements listed in Table 30-4. Their safety has been demonstrated in over 30 years or historical use in the healthcare industry. Polydimethylsiloxane derivatives, which are now approved in various pharmaceutical products, have achieved the status of pharmacopoeial excipients. Specifically, the unique properties of the polydimethylsiloxane chain permits the silicone adhesives to be very suitable for use in transdermal drug delivery applications. Their biocompatibility is due in part to their surface activity and hydrophobicity which dramatically limits their interactions with body fluids and provides for their excellent chemical stability.

In addition, silicone pressure sensitive adhesives can conform to the stratum corneum and accommodate skin movement because of both their viscoelastic properties and their ability to wet and to spread on moist surfaces. Moreover these silicones do not contain additives such as antioxidants, tackifiers, plasticizers and other potential extractables.

Drug Compatibility and Release

Silicone pressure sensitive adhesives can be designed to be loaded with drugs and galenic excipients to achieve the required drug release profiles. As shown in Figure 30-3, the drug can be formulated into either an adhesive matrix (first-order release rate), or a reservoir type system (zero-order release rate) for transdermal drug delivery systems. The high permeability of silicone polymers to a wide variety of therapeutic molecules (progesterone, testosterone, propranolol and indomethacin [15]) and gases (oxygen and water vapor), make them especially attractive for both types of transdermal drug delivery systems. Their permeability is directly linked to the open macromolecular structure of polydimethylsiloxane which contains large free volume that facilitate molecular diffusion. The solubility of drugs in silicone adhesives can be estimated based upon solubility parameters and Hildebrand values. For instance, the lower the Hildebrand solubility of the active drug, the higher is its solubility in silicone pressure sensitive adhesive.

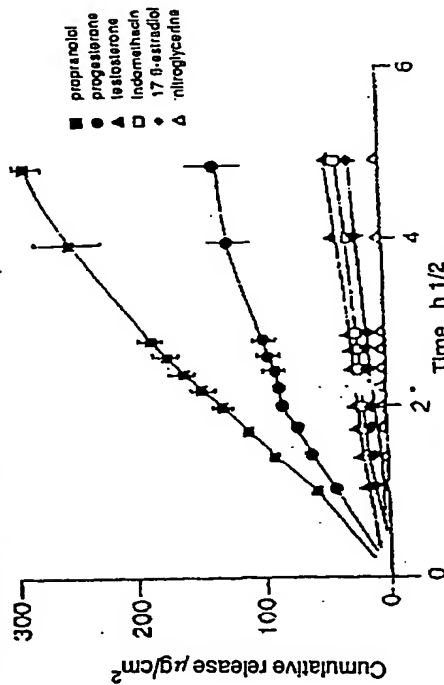


Fig. 30-4. Release kinetics of drugs from silicone pressure sensitive adhesives (BIO-PSA, which is a registered trademark of the Dow Corning Corporation).

Figure 30-4 shows the release profile for six different drugs through a standard, medium tack silicone adhesive [7].

Due to the lipophilicity of polydimethylsiloxane, each drug exhibits a different behavior and drug release profile. The solubility and the diffusion of drugs through the silicone adhesive matrix can be improved by coformulating the drug loaded silicone adhesive matrices with an appropriate combination of cosolvents, permeation enhancers and resins [16,17]. However, by acting as a solvent (Hildebrand solubility parameter below $9.9 \text{ cal}^{1/2}/\text{cm}^{3/2}$), excessive levels of some liquid substances can plasticize the silicone adhesives. In order to minimize the effect of cold flow and cohesive failure, the silicone adhesives may require further resin reinforcement or polymer crosslinking. Numerous studies have supported both the efficacy and suitability of silicone adhesives in transdermal drug delivery applications [7,18,19,20].

Medical Device Applications

Various medical device applications have utilized both the physical and chemical property characteristics of silicone pressure sensitive adhesives. These applications include adhesion for wound care management, ostomy appliances, diagnostic devices, and intravenous tube holders [21]. Some of the advantages of silicone adhesives can be seen in their high permeability to oxygen and excellent biocompatibility (including low levels of potential contaminants). In addition to medical devices, these adhesives are often used in non-medical applications which require the adhesion of prosthetic devices to the body. These applications have included use in securing molded character masks and facial appliances on TV and film actors as well as applying toupees and wigs to hair care clients.

Manufacturing

In addition to having different physical property requirements (lower adhesion and cohesive strength) and chemical property requirements (biological and chemical inertness) than industrial adhesives, adhesives targeted for the healthcare industry must also be manufactured in accordance with Good Manufacturing Practices (GMP). Also, if the adhesives are to be used in pharmaceutical systems (such as transdermal drug delivery) or medical devices, emerging regulatory practices may require the manufacturing processes and products to be validated.

Completing the initial synthetic steps outlined in Figure 30-2 yields soluble standard silicone pressure sensitive adhesives which often contain a significant level of residual silanol functionality. These silanols are prone to further reaction or hydrogen bonding in the presence of amino functional substances. Further condensation can result in highly crosslinked, dry, rubbery materials which display little or no pressure sensitive properties. To prevent and/or minimize such behavior, the residual silanol functionality can be capped with trimethylsiloxy groups, thus yielding amine compatible adhesives.

With or without trimethylsilyl endcapping, the polycondensation reaction yields a soluble, high molecular weight polymer network which exhibits the rheological characteristics of pressure sensitive adhesives when 50 to 70 percent resin by weight is incorporated into the formulation.

Commercialization

Using the silicone technology outlined in Figure 30-2, Dow Corning Corporation has developed two families of silicone pressure sensitive adhesives for use by the healthcare industry. The first family is comprised of the standard silicone pressure sensitive adhesives (former Dow Corning 355 Medical Adhesive type) and the second family consists of amine compatible silicone pressure sensitive adhesives (former BIO-PSA Q7-2920 type). Both families can be formulated to meet various performance properly profiles (based on resin/polymer ratio and degree of crosslinking) as well as different processing parameters (e.g. type and concentration of solvent). These silicone pressure sensitive adhesives are designed to flow under light pressure at skin temperature and to conform to the skin [22,23].

In addition to utilizing some of the commercial standard adhesive formulations to apply prosthetic devices, custom formulations of adhesive from both families have been successfully developed and commercialized for use in transdermal drug delivery systems (e.g. Transderm-Nitro from Ciba-Geigy Corporation and Duragesic from Janssen Pharmaceutica, Inc.). Transderm-Nitro is a drug reservoir system which delivers nitroglycerine for 24 hours and utilizes the adhesive as the contact adhesive layer. In the Duragesic system, the silicone adhesive is laminated to the face of a rate controlling membrane.

FUTURE POTENTIAL AND EMERGING DEVELOPMENTS

Hot Melt Silicone Adhesives

New and emerging environmental regulations are limiting the use and/or emissions of various solvents (e.g. Montreal Protocol - organic halogenated derivatives; various countries and states-volatile organic compounds); therefore, an increase in the interest of solventless pressure sensitive adhesives has been taking place. In an attempt to meet this demand, new generations of hot melt silicone pressure sensitive adhesives have been investigated.

Hot melt pressure sensitive adhesives are those adhesives, which upon heating neat, soften to viscosities suitable for coating. Although these adhesives soften to viscosities suitable for coating at elevated temperatures (typically between 50°C to 200°C), it is required that they return to a generally flowless state upon cooling. The advantages for using hot melt pressure sensitive adhesives are:

- They do not require solvent removal or disposal.
- They do not require special flammable ratings for either the products and/or the coating processes.
- They allow for the use of smaller, less expensive and more energy efficient coating equipment.
- They are more easily coated into thick sections with minimal bubbling, a problem which often results from coating thick sections of solventborne adhesives.

In summary, they can be coated and laminated into silicone adhesive matrices or tapes by avoiding the expensive, cumbersome and often dangerous use of flammable solvents.

Hot melt silicone pressure sensitive adhesives can be prepared by the addition of plasticizers. The resulting physical properties and potential drug delivery rates are dependent on both the concentration of the plasticizer (typically 1 to 15 weight percent) and type of plasticizer used (e.g. organic esters, nonflammable hydrocarbon fluids, organic waxes, polyphenylmethylsiloxane fluids, alkylmethylsiloxane waxes and siloxylated allyloxopropane diols). The plasticizers can be either blended into the silicone network or they can be linked to the silicone polymer matrix. The plasticizing agents typically decrease both the dynamic viscosity and the elastic modulus of the adhesive matrix, thus allowing the silicone adhesives to flow under pressure at elevated temperature (120°C), while maintaining their cohesive and adhesive properties at skin temperature. Tables 30-5 through 30-10 provide both the physical tape properties of release (g/cm), adhesion (g/cm) and shear (kg/6.3 cm²). Adhesive properties were determined using Dow Corning Corporate test methods on tapes composed of polyester backing, an adhesive (0.05 mm thick), and Scotchpak 1022 release liner, as well as dynamic mechanical viscosity values between 50 - 200°C using a Rheometrics Dynamic Spectrometer, Model RDS2 and running a temperature sweep on 10 gram samples of 1 mm thickness and operating the tester at a frequency of 10 radians/second at a 1% strain using a 50 mm cup and plate for potential hot melt adhesives formulations.

REDUCED COLD FLOW SILICONE ADHESIVES

Typically, when silicone adhesives are formulated with cosolvents, excipients, certain drugs (e.g. nicotine), or skin penetration enhancers (e.g. polypropylene glycol monolaurate or glycerol monooleate), they are often plasticized and can lose their resistance to flow, thus resulting in enhanced cold flow or creep properties. Cold flow or creep refer to the viscoelastic flow of the adhesive under stress [31]. Various techniques have been investigated in an attempt to improve the creep resistance of silicone pressure sensitive adhesives. Some of these techniques are reviewed below.

Table 30-5. Amino Compatible Silicone PSAs with Organic Esters [24]

| ESTER TYPE | ESTER CONTENT wt. % | TAPE PROPERTIES | | DYNAMIC VISCOSITY | |
|--------------------------|---------------------|-----------------|---------------|-------------------|---------|
| | | RELEASE g/cm | ADHESION g/cm | 100°C P | 200°C P |
| Control | 1 | 1 | 650 | 14,000 | 500 |
| Dodecyl acetate | 5 | 20 | 470 | 1,300 | 213 |
| Ethyl triconcanoate | 5 | >1 | 410 | 1,400 | 189 |
| Octyl acetate | 5 | 4 | 540 | 1,800 | 250 |
| Methyl caproate | 5 | 5 | 530 | 3,100 | 210 |
| Methyl decanoate | 5 | 4 | 620 | 470 | 150 |
| Isobutyl acetate | 5 | 18 | 370 | 2,400 | 165 |
| Methyl heptadecanoate | 5 | 11 | 840 | 560 | 133 |
| Isopropyl palmitate | 5 | 11 | 250 | 740 | 165 |
| 1-phenylethyl propionate | 5 | <1 | 720 | 2,000 | 217 |

Table 30-6. Silicone Pressure Sensitive Adhesives with Nonflammable Hydrocarbon Fluids [25]

| FLUID | FLUID CONTENT wt. % | TAPE PROPERTIES | | DYNAMIC VISCOSITY | |
|---------------------------------|---------------------|-----------------|---------------|-------------------|---------|
| | | RELEASE g/cm | ADHESION g/cm | 100°C P | 200°C P |
| Control (amine compatible PSAs) | 0 | 2 | 720 | 45,400 | 1,200 |
| light mineral oil | 5 | 17 | 550 | 3,000 | 200 |
| light mineral oil | 10 | 12 | 110 | 900 | 100 |
| heavy mineral oil | 5 | 18 | 560 | 4,300 | 270 |
| heavy mineral oil | 10 | 12 | 90 | 1,300 | 92 |
| petrolatum | 5 | 8 | 320 | 6,000 | 253 |
| petrolatum | 10 | 9 | 170 | 3,500 | 133 |
| Control (standard PSA, Type 1) | 0 | 3 | 720 | 78,500 | 1,600 |
| light mineral oil | 5 | 9 | 300 | 7,000 | 500 |
| heavy mineral oil | 5 | 10 | 420 | 1,000 | 700 |
| petrolatum | 5 | 6 | 340 | 12,800 | 700 |
| Control (standard PSA, Type 2) | 0 | 8 | 670 | 50,600 | 10,700 |
| light mineral oil | 5 | 6 | 220 | 22,400 | 6,200 |
| heavy mineral oil | 5 | 6 | 230 | 25,600 | 7,400 |
| petrolatum | 5 | 6 | 310 | 28,300 | 6,600 |

Table 30-7. Standard Silicone PSAs with Phenyl Containing Silicone Fluids [26]

| POLYPHENYLMETHYL COPOLYMER ≈ 22.5 cSt | FLUID CONTENT wt. % | TAPE PROPERTIES | | DYNAMIC VISCOSITY | |
|---|---------------------------|-----------------|----------|-------------------|-------|
| | | RELEASE | ADHESION | 100°C | 200°C |
| | | g/cm | g/cm | P | P |
| Control, PSA, type 1 | | | | | |
| | 0 | | | ND | |
| | 5 | | | 96,000 | 1,300 |
| | 10 | | | 40,000 | 1,200 |
| | 15 | | | 15,000 | 720 |
| Control, PSA, type 2 | | | | | |
| | 0 | 10 | 555 | | |
| | 5 | 11 | 474 | | |
| | 10 | 14 | 492 | | |
| | 15 | 14 | 482 | | |

Table 30-8. Amine Compatible Silicone Pressure Sensitive Adhesives Plasticized with Alkylmethyl Siloxane Waxes [27,28]

| WAX TYPE | WAX CONTENT | TAPE PROPERTIES | | DYNAMIC VISCOSITY | |
|---|----------------|-----------------|----------|-------------------|-------|
| | | RELEASE | ADHESION | 50°C | 100°C |
| | | g/cm | g/cm | P | P |
| Control | | | | | |
| | 0 | 3 | 570 | 15.8 | 6,700 |
| | 5 | 6 | 500 | 13.2 | 3,100 |
| | 10 | 9 | 190 | 12.5 | 5,900 |
| | 15 | 5 | 610 | 11.8 | 1,900 |
| (C ₁₈ H ₃₇ SiO) ₄ mp -38°C | | | | | |
| | 0 | 3 | 570 | 15.8 | 6,700 |
| | 5 | 6 | 500 | 13.2 | 3,100 |
| | 10 | 9 | 190 | 12.5 | 5,900 |
| | 15 | 5 | 610 | 11.8 | 1,900 |
| (C ₂₀ H ₄₁ SiO) ₃ mp -53°C | | | | | |
| | 5 | 3 | 620 | 13.5 | 3,100 |
| | 10 | 10 | 400 | 9.1 | 5,400 |
| | 15 | 17 | 560 | 5.1 | 3,200 |
| (C ₂₄ -28H ₅₉₋₅₇ MeSiO) ₃ mp -56°C | | | | | |
| | 5 | 3 | 650 | 14.5 | 2,500 |
| | 10 | 12 | 440 | 10.5 | 4,700 |
| | 15 | 17 | 330 | 5.8 | 4,000 |
| Linear copolymer mp -48°C | | | | | |
| | 5 | 14 | 510 | 9.1 | 4,100 |
| | 10 | 8 | 200 | 12.1 | 5,600 |
| | 15 | 3 | 522 | 13.4 | 1,300 |

Table 30-9. Silicone Pressure Sensitive Adhesives Plasticized with Organic Waxes [29]

| WAX TYPE | WAX CONTENT | TAPE PROPERTIES | | DYNAMIC VISCOSITY | |
|--------------------------------|----------------|-----------------|----------|-------------------|-------|
| | | RELEASE | ADHESION | 50°C | 100°C |
| | | g/cm | g/cm | P | P |
| Control (amine compatible) | | | | | |
| | 0 | 3 | .730 | 16.7 | 6,800 |
| Ozokerite Sp1026 (mineral wax) | | | | | |
| | 5 | 7 | 420 | 14.7 | 6,400 |
| | 10 | 4 | 560 | 13.3 | 6,800 |
| | 15 | 6 | 470 | 13.8 | 6,600 |
| Carnauba (vegetable wax) | | | | | |
| | 5 | 9 | 410 | 16.0 | |
| | 10 | 4 | 250 | 13.5 | 6,600 |
| | 15 | 3 | 230 | 15.0 | 4,700 |
| Ceresine Sp1022 (mineral wax) | | | | | |
| | 5 | 4 | 430 | 13.4 | 6,800 |
| | 10 | 8 | 340 | 14.0 | 6,100 |
| | 15 | 5 | 500 | 14.6 | 5,400 |
| Control (standard PS, Type 1) | | | | | |
| | 0 | <1 | 880 | 14.6 | 6,900 |
| Ozokerite Sp1026 | | | | | |
| | 10 | 0 | 440 | 16.2 | 6,200 |
| | 5 | 0 | 270 | 14.0 | 6,800 |
| | 10 | <1 | 170 | 15.2 | 7,100 |
| | 15 | <1 | 80 | 14.5 | 3,300 |
| Ceresine Sp1022 | | | | | |
| | 5 | <1 | 590 | 16.9 | 3,900 |
| | 10 | <1 | 570 | 15.3 | 6,500 |
| | 15 | <1 | 630 | 13.6 | 6,300 |
| Control (standard PSA, Type 2) | | | | | |
| | 0 | 3 | 680 | 18.4 | 5,100 |
| Ozokerite Sp1026 | | | | | |
| | 10 | 8 | 540 | 13.5 | 6,400 |
| | 5 | 16 | 340 | 14.4 | 6,800 |
| | 10 | 3 | 400 | 15.9 | 6,900 |
| | 15 | 1 | 130 | 12.8 | 6,400 |
| Ceresine Sp1022 | | | | | |
| | 5 | 16 | 510 | 13.9 | 5,800 |
| | 10 | 9 | 430 | 13.6 | 5,200 |
| | 15 | 12 | 340 | 13.5 | 6,500 |

Table 30. Silicone PSAs Plasticized with Siloxylated Allyloxypropane Diols [30]

| DIOL TYPE | DIOL CONTENT wt. % | TAPE PROPERTIES | | | DYNAMIC VISCOSITY | |
|--------------------------------------|--------------------|-----------------|---------------|------------------------------|-------------------|-------|
| | | RELEASE g/cm | ADHESION g/cm | SHEAR kg/6.3 cm ² | 50°C | 200°C |
| Control, standard PSA, Type 1 MD'M* | 0 | 1 | 555 | 17.0 | nd | - |
| | 10 | 2 | 242 | 11.0 | 6,800 | 250 |
| Control, amine compatible PSA Type 1 | 0 | 3 | 720 | 15.3 | 6,500 | 1000 |
| MD'M | 10 | 4 | 130 | 2.0 | 5,300 | 240 |
| Control, amine compatible PSA Type 2 | 0 | 16 | 210 | 8.0 | 16,000 | 310 |
| MD'M | 10 | 6 | 155 | 7.0 | 15,000 | 270 |
| MD'83M | 10 | 7 | 300 | 7.5 | 19,000 | 230 |
| MD41.5D'83M | 10 | 7 | 320 | 6.4 | 20,000 | 220 |
| MD166D'83M | 10 | 8 | 260 | 8.2 | 18,000 | 280 |
| Control, standard PSA, Type 2 | 0 | 13 | 310 | 4.5 | 66,000 | 190 |
| MD'M | 10 | 7 | 520 | 7.1 | - | - |
| MD'83M | 10 | 10 | 310 | 3.0 | 13,000 | 340 |
| MD41.5D'83M | 10 | 8 | 370 | 3.2 | - | - |
| MD166D'83M | 10 | 9 | 360 | 2.7 | 16,000 | 290 |

* Where M represents $(CH_3)_2SiO$ or $(CH_3)_3Si$ endcapping groups.

D represents $(CH_3)_2SiO$ repeat units.

D' represents $(CH_3)_2OCH_2CH(OH)CH_2OH[SiO]$ repeat units.

Cohesive Strengthening Agents

Various nonionic surfactants, fatty acid esters of glycerol, metallic salts of fatty, phosphoric, and carbonic acids, polysaccharides, carboxypolyethylene, polyvinylpyrrolidone, polyvinylalcohol and amorphous precipitated silicas have been evaluated as cohesive strengthening agents for silicone pressure sensitive

adhesives [32]. Results have shown that 1 to 10 weight percent calcium stearate provides reinforcement of the silicone adhesive, while maintaining adequate adhesive properties and imparting creep resistance proportional to the loading level of calcium stearate in the adhesive. Both ethyl cellulose (a pharmaceutical thickening agent with a high degree of hydrogen bonding) and magnesium stearate (a pharmaceutical excipient used as a lubricant in oral dosage forms) have been shown to be effective at reducing the flow properties of standard silicone pressure sensitive adhesives. As with the calcium stearate, the degree of creep resistance is proportional to the additive loading level, the optimum loading being 10 to 20 weight percent.

Crosslinkable Silicone Elastomer

In an attempt to impart better creep resistance, low viscosity and homogeneous formulations of silicone pressure sensitive adhesive compositions, crosslinkable silicone elastomer compositions and optionally a viscosity reducing agent have been investigated [33]. Some advantages of these formulations are:

- they are devoid of flammable solvents, yet they have low enough viscosity for room temperature molding techniques;
- they can be cured at room or reduced temperatures;
- they have formulation flexibility (e.g. they can be formulated with or without fillers and with various crosslinkable silicone elastomer compositions and still yield a low-viscosity, moldable composition);
- they can significantly reduce the adhesive cold flow, even in the presence of strong plasticizers (e.g. enhancers, excipients, or drugs).

Platinum Cured Adhesives

Similar to the crosslinkable silicone elastomer compositions described above, two part, low viscosity, platinum cured silicone adhesives have been investigated. These adhesives can be cured at reduced temperatures (cure rate can be accelerated with heat). By varying the degree of crosslinking, the resin and polymer molecular weights, and the resin-to-polymer ratio, adhesive properties can be optimized to meet most applications targeted towards the healthcare industry (e.g. wound dressings, bandages, prosthetic attachment, and transdermal drug delivery systems).

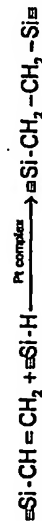
Two Part Silicone Adhesive Gels

Another solution for reducing the cold flow and improving the cohesiveness of solventless pressure sensitive materials is to base their structure on a highly crosslinked system such as an elastomer or gel. For years silicone elastomers have played a major role in the manufacture of medical devices for the healthcare industry (e.g. prosthesis, tubing, and drug delivery systems) [34]. Silicone elastomers are crosslinked polydimethylsiloxane polymers which are reinforced with fillers. Silicone gels differ from analogous elastomers by the absence of reinforcing silica. In addition, although crosslinked, these gels are typically very soft and often require other mechanical measures to impart durability. Currently, silicone gels are used to fabricate soft, cohesive devices which display resilient character.

As such, silicone gels have been commercialized in wound care applications. For instance, Smith & Nephew has commercialized a gel sheeting (Cica-care) which has been shown to soften and reduce hypertrophic scars. Silicone gels have also been recognized as a vehicle for sustained drug release in the design of new drug-loaded wound dressings [38].

Based on gel technology, silicone adhesive gels have been developed to provide a self-adhesive matrix which can be used when a soft and cohesive adhesive is required for skin contact. Silicone adhesive gels combine the tack properties of silicone pressure sensitive adhesives and the advantages of an elastomeric network. They can be loaded with drugs and excipients without suffering plasticizing effects.

In terms of chemistry, the silicone adhesive gels are currently two-part systems based on a vinyl functional polydimethylsiloxane and a hydrogen crosslinker. As shown below, platinum is used to catalyze the system.



Silicone gels exhibit the following properties and characteristics:

- Solventless, low viscosity two part systems
- Room temperature and heat accelerated cure
- High degree of softness and resilience
- Optically clear before and after curing
- Easily custom formulated

SILICONE PSAs FOR HEALTHCARE APPLICATIONS 745

Silicone pressure sensitive adhesives are typically coated onto a release liner, dried (to remove the solvent) and laminated to the backing substrate; however, silicone adhesive gels must be coated and cured directly onto the backing substrate in order to eliminate the potential or chemical interaction with the release liner. Although silicone pressure sensitive adhesives require a low energy surface for release (e.g. fluorocarbon or fluorosilicone), silicone adhesive gels can utilize polyethylene films as release liners.

Hydrophilic Silicone Pressure Sensitive Adhesives

Although polydimethylsiloxane adhesives demonstrate a high degree of solubility and permeability to various lipophilic drugs [35] (because of the hydrophobic nature of the PDMS polymer), solubility and diffusion of lipophilic drugs are limited. Thus, silicone pressure sensitive adhesives may require some modification in order to improve both the drug solubility and permeation rate of certain drugs. As discussed previously for the hot melt adhesive, these modifications can take various forms. For example, one can change the hydrophilic nature of the adhesive by formulating with hydrophilic fillers [32,39], copolymers [30], or plasticizers [24]. In addition, the hydrophilicity of the polymer network can be modified through the use of hydrophilic silicone-organic copolymers. Earlier work has demonstrated that polydimethylsiloxane/polyethylene oxide graft copolymers can lead to a new family of silicone pressure sensitive adhesives with unique permeability and solubility for hydrophilic drugs while maintaining acceptable pressure sensitive characteristics [36,37]. The greatest advantage of using hydrophilic copolymers to enhance the hydrophilic nature of the network is that it eliminates and/or minimizes the potential for excessive loading of hydrophilic excipients which could alter the physical properties of the adhesive (e.g. cold flow).

REFERENCES

1. Noll, W., *Chemistry and Technology of Silicones*. Academic Press Inc., New York, 1968.
2. Collas, André, *Les Silicones: Préparation et Performances*. Chimie Nouvelle, 8(30), 847-852 (1990).
3. Owen, Michael J., *Chemtech*, 11, 288-292 (1981).
4. Sobieski, L. A. and Tanguay, T. J., *Silicone Pressure Sensitive Adhesives. Handbook of Pressure Sensitive Adhesive Technology*. (D. Satas, ed.). 2nd ed., Van Nostrand Reinhold, New York, 1989, 508-517.

5. Merrill, D. F., *Silicone Pressure Sensitive Adhesives*. Handbook of Pressure Sensitive Adhesive Technology, (D. Szaas, ed.) Van Nostrand Reinhold, New York, 1982, 344-352.
6. Woodard, J. T. and Metevia, V. L., U. S. Patent 4,655,767 (1987)(assigned to Dow Corning Corporation).
7. Mariani, D. S. et al., *Proc. Intern. Symp. Control. Rel. Bioact. Mater.*, 14, 265-266 (1987).
8. Pfister, W. R., *Adhesives Age* 33 (13) 20-24 (1990).
9. Arkles, B. and Redinger, R., *Silicones in Biomedical Applications*. Biocompatible Polymers, Metals and Composites, (M. Szycher, ed.). Technomic Publishing Co. Inc., Lancaster, PA, 1983, 749-768.
10. Huie, S., Schmitt, P. F., and Warren, J.S., *Adhesive Age* 28 (9) 30-35 (1985).
11. Sobieski, L.A. and Tuguey, T. J., *Adhesives Age* 31 (11) 23-26 (1988).
12. Hadgraft, Johnathan and Guy, Richard H., *Drugs and the Pharmaceutical Sciences*, 35 (1989).
13. Chien, Yie W., *Drugs and the Pharmaceutical Sciences*, 31(1987).
14. Pfister, W. R., Woodward, J. T. and Grigoras, S., *Pharmaceutical Technology*, 16 (1), 42-58 (1992).
15. Pfister, W. R. et al., *Proc. Int. Symp. Control. Rel. Bioact. Mater.*, 14, 223-224 (1987).
16. Pfister, William R. and Hsieh, Dean S., *T. Pharmaceutical Technology*, 14(9), 132-140 (1990).
17. Pfister, William R. and Hsieh, Dean S., *T. Pharmaceutical Technology*, 14 (9) (1990).
18. P. Catz, et al., *Int. Symp. Control. Rel. Bioact. Mater.*, 16, 175-176 (1989).
19. Roy, S. et al., *Rel. Bioact. Mater.*, 16: 41-42 (1989).
20. Choi, S.H. et al., *Proc. Int. Symp. Control. Rel. Bioact. Mater.*, 17, 100-101(1990).
21. Krug, Ken and Marecki, Nelda M., *Adhesives Age* 26, 19-23 (1983).
22. Pfister, William R., *Drug and Cosmetic Industry*, 143 (4) 44-52 (1988).
23. Pfister, William R., *Pharm. Tech.*, 13 (3), 126-138, (1989).
24. Sweet, Randall P., *US Patent 5,865,920* (1989) (assigned to Dow Corning Corporation).
25. Sweet, Randall P., *US Patent 5,147,916* (1992) (assigned to Dow Corning Corporation).
26. Sweet, Randall P., *US Patent 5,162,410* (1992) (assigned to Dow Corning Corporation).
27. Sweet, Randall P., Durfee, Loren D., and Ulman, Katherine L., *US Patent 5,300,299* (1994) (assigned to Dow Corning Corporation).
28. Sweet, Randall P., Durfee, Loren D., Ulman, Katherine L. and Noel, Ross A., *US Patent 5,352,722* (1994) (assigned to Dow Corning Corporation).
29. Noel, Ross A., *US Patent 5,328,696* (1994) (assigned to Dow Corning Corporation).
30. Ulman, Katherine L., Schulz, William J., and Keryk, John R., *US Patent 5,371,128* (1994) (assigned to Dow Corning Corporation).
31. Dahlquist, Carl A., *Creep Handbook of Pressure Sensitive Adhesive Technology* (D. Szaas, ed.) 2nd ed. Van Nostrand Reinhold, New York, 1989, 97.
32. Pfister, William R. and Wilson, Jennifer M., *US Patent 5,232,702* (1993) (assigned to Dow Corning Corporation).
33. Sweet, Randall P., Miller, Patrick J., and Metevia, Virgil L., *US Patent 4,882,377* (1989) (assigned to Dow Corning Corporation).
34. Thomas, Xavier and Pfister, William R., *STP Pharma Sciences*, 1(1), 38-46(1991).
35. Toddewala, R. and Chien, Y.W., *Drug Developmental and Industrial Pharmacy* 17(2), 245-269(1991).

36. Ulman, K.L., Lee, Chi-Long, J., *Cont. Rel.*, 1989.
37. Lee, Chi-Long and Ulman, K.L., *US Patent 4,898,920* (1990) (assigned to Dow Corning Corporation).
38. Sawada, Y. et al., *Brit. J. Plastic Surgery* 43, 78-82(1990).
39. *European Patent 0465 744 A1* (1990) (assigned to Dow Corning France).